AMERICAN JOURNAL OF PHYSICAL ANTHROPOLOGY 106:515–520 (1998)

Immunology and Growth Faltering of Anga Children, Papua New Guinea: Preliminary Work

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KEY WORDS leucocytes; infection; anthropometry; nutritional status; immunology

ABSTRACT Nutrition–infection interactions among poor children of the less-developed world influence growth and development. However, the relative importance of each is difficult to determine, because the relationship is mediated by immunological status. In this analysis, relationships between immunological measures and anthropometry were sought among 41 Anga, Papua New Guinea children aged 0–7 years. These had elevated serum total leucocyte and leucocyte subset counts relative to western reference values. Although there was no correlation between anthropometric nutritional status and total leucocytes and leucocyte subsets for this group, the small group (n = 8) with very high total leucocyte count (greater than 15,000/mm^2) had significantly lower mean Z score of stature for age (−3.78), and weight for stature (−1.35) than those with leucocyte counts lower than this cut-off (weight for stature Z score: −0.59; stature for age Z score: −2.68, respectively. Low stature-for-age Z score was associated with lower total lymphocyte count and increasing age, against a background of elevated lymphocyte levels relative to western reference values among the older children; low weight-for-stature Z score was associated with lower neutrophil count, against a background of normal neutrophil levels across all age groups. The pattern of weight and stature growth seen in the Anga may reflect extended nutritional deficits which result in stunting of a degree to which the most growth-compromised children die, leaving those above a threshold associated with high mortality alive. Thus, the anthropometric and immunological characteristics of the older children in this small sample may reflect the biology of survival under severe ecological conditions, where poor linear growth and elevated leucocyte status relative to normative values are characteristics of survivorship. Am J Phys Anthropol 106:515–520, 1998.

Among children in developing countries, repeated infections can elevate as well as suppress the immune response, making the interpretation of nutrition–infection interactions difficult. This problem of interpretation is most pronounced in areas of high and stable disease prevalence, where immunological stress might play an independent role in the growth faltering usually associated with undernutrition. In this article, serum leucocyte profiles are examined for a small group of Anga, Papua New Guinea (PNG), children aged 0–7 years, from a population known to undergo growth faltering (Ulijaszek, 1981), and which experiences nutritional (Saweri, 1995) and infectious disease stress. The sample excluded all chil-

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Received 17 September 1997; accepted 5 March 1998.

dren with apparent infections at the time of survey. Leucocytes and their subsets are compared with western reference values which reflect the uninfected state, to determine age dependency of immune status, and with anthropometrically determined nutritional status to examine relationships between undernutrition and immune status in this population.

MATERIALS AND METHODS

The Anga people, formerly known as "Kukukuku," number approximately 70,000 and live in a highland fringe area overlapping three provinces of Papua New Guinea, Gulf, Morobe, and Eastern Highlands Provinces, respectively. They are predominantly taro and sweet potato horticulturalists who have had very little experience of modernization and economic development. High rates of anthropometrically assessed undernutrition (Heywood, 1985) and infant and 1- to 5-year mortality determined from rural maternal and child health clinic records (Leonard et al., 1988) have been reported for Anga of all three provinces. Furthermore, Anga children undergo severe nutritional wasting in association with stunting between the ages of 6 and 30 months (Ulijaszek, 1996). Experience of infectious disease includes parasitic infections such as hookworm and ascariasis (Ashford et al. 1981), as well as malaria (Cattani, 1992), acute respiratory infection (Riley, Lehman and Alpers, 1992), and diarrheal infections typical of similar-altitude zones elsewhere in PNG. Hookworm and ascariasis prevalence has been determined by examination of fecal samples for worm and egg loads, whereas malaria prevalence has been ascertained by assessment of spleen size and passive case detection. Records of respiratory infection and diarrhea come from health post records and outpatient treatment reports of Kanabea Hospital, Gulf Province.

In this study, lengths, heights, and weights of an opportunity sample of young Anga children in Gulf Province, all without apparent infection, were measured using standard methods (Weiner and Lourie, 1981). Lengths were measured in children below the age of 18 months, heights in children above this age. The term "stature" is used to reflect length measurements in children below 18 months of age, and height measurements in children above this age. Z scores of stature for age (S/A) and weight for stature (W/S) were calculated using National Center for Health Statistics (1977) reference data for comparison. Although it might be preferable to use local reference values based on measurements of elite Papua New Guinea children for comparison, such data do not exist. This study was part of a larger one of nutritional status carried out in the Gulf Province in 1980–1981 (Ulijaszek, 1981), and only children with known ages were included in the present analysis. Ages were determined from clinic record cards, and were accurate to within 2 weeks. Immune function was examined by serum estimates of total leucocyte counts, and counts of total lymphocytes (T and B cells combined) and neutrophils in a sample of 41 children. Counts of monocytes, basophils, and eosinophils combined were determined by the arithmetic difference between total leucocyte count and counts of lymphocytes and neutrophils. Upon collection, blood was transported by air to Port Moresby, where leucocyte counts were determined using a counterchamber at Port Moresby General Hospital. Comparisons between age groups were made using Student t-tests of logarithmically transformed data where appropriate. Stepwise multivariate analyses, setting variables in at $P < .10$, were carried out using the Statistical Package for the Social Sciences for Portable Computer.

TABLE 1. Number of children in the sample, by age group and sex

Age group (years)	Male	Female
0–0.9	6	4
1–1.9	7	4
2–2.9	4	3
3–3.9	3	1
4–4.9	2	3
5–5.9	0	2
6–6.9	1	1
Total	23	18

RESULTS

Table 1 gives the distribution of the sample by age group and sex. There were slightly more males than females, with similar distri-

TABLE 2. Leucocyte count (cells/mm²) and nutritional status

	Age group (years)			
	0–1.9	2–7		
Sample size	21	20		
Immunology: Mean (SD)				
Total leucocyte count	12,821 (4,269)	12,340 (4,759)	0.53[1,2]	
Total lymphocytes	7,057 (2,234)	6,384 (2,806)	1.06[1,2]	
Neutrophils	3,782 (1,398)	3,922 (1,484)	0.52[1,2]	
Monocytes, eosinophils, and basophils combined	1,932 (1,641)	1,538 (866)	1.30[1,2]	
Nutritional status				
Z S/A	−2.57 (0.74)	−3.28 (0.67)	3.22[2]	$P < .01$
Z W/S	−0.86 (0.84)	−0.62 (0.53)	1.10[2]	

[1] Based on comparisons of means using logarithmically transformed data.
[2] Student's t-test.

TABLE 3. Leucocyte count as a percentage of reference values (from Lentner, 1984)[1]

	Age group	
	0–1.9 years (%)	2–7 years (%)
Total leucocytes	112	140
Total lymphocytes	101	160
Neutrophils	108	97
Monocytes, eosinophils, and basophils combined	221	295

[1] Cells/mm².

*TABLE 4. Relationships between anthropometric nutritional status and immunological count (correlation coefficients), age groups pooled**

	S/A[1]	W/S[1]
Total leucocytes	0.07[2]	−0.06[2]
Total lymphocytes	0.24[2]	−0.15[2]
Neutrophils	−0.17[2]	0.11[2]
Monocytes, eosinophils, and basophils combined	0.10[2]	−0.14[2]

* All correlations nonsignifcant.
[1] Nutritional status.
[2] Correlation coefficients.

butions across age groups, but with females having slightly greater mean age (2.8 years) than males (2.2 years). Table 2 gives mean counts for leucocyte and leucocyte subsets, and Z scores of S/A and W/S, whereas Table 3 gives values for leucocytes and leucocyte subsets expressed as a percentage of reference values (Lentner, 1984), in children aged 0–2 and 2–7 years, respectively. There was no significant difference between leucocyte counts between the younger and older age groups. This is in contrast to the decline in leucocyte number found among healthy western populations who experience little exposure to infectious disease. In this sample, the vast majority of nutritional stunting takes place within the first 2 years of life, and mean Z S/A was significantly lower in the 2–7 years age group than in the 0–2 years age group. There was no significant difference in Z W/S between the younger and older age group, indicating that nutritional wasting persists beyond the age of 2 years. Total leucocyte count was slightly elevated relative to western reference values in the 0–1.9 years age group, but was 40% above reference values in the 2–7 years age group. Dissaggregating this into leucocyte subsets, the slightly elevated total leucocyte value in the 0–1.9 years age group was due to a small elevation in neutrophil number, and a large elevation in the number of monocytes, eosinophils, and basophils combined. Comparing the older age group with the younger one, the elevated number of total leucocytes in the older age group was due to elevated values for total lymphocytes and monocytes, eosinophils, and basophils combined. The sum total of monocytes, eosinophils, and basophils showed the greatest elevation relative to reference values for both age groups.

Although associations between leucocyte counts and Z scores of S/A and W/S were sought using Pearson correlation coefficients and none were found (Table 4), the small group of children with total leucocyte count above 15,000 had significantly lower S/A ($P < .001$) and W/S ($P < .02$) (Table 5). Multivariate analysis using immunological measures as dependent variables and age, sex, and anthropometry as independent variables (Table 6) showed some weak, but interesting associations. Total leucocyte count was independent of age, sex, Z S/A, and Z W/S, whereas total lymphocyte count was significantly associated with Z S/A and age,

TABLE 5. Weight-for-stature and stature-for-age Z scores of Anga children with total leucocyte count greater than 15,000, age groups pooled

	Leucocyte count			
	>15,000	<15,000		
Sample size	8	33		
Mean age (years)	2.51	2.30		
(females/males)	4/4	14/19		
W/S Z score				
Mean	−1.35	−0.59	2.59[1]	$P < .02$
(SD)	(0.78)	(0.58)		
S/A Z score				
Mean	−3.78	−2.68	4.29[1]	$P < .001$
(SD)	(0.63)	(0.73)		

[1] Student's t-test.

TABLE 6. Stepwise multiple regression: factors influencing leucocyte count

Independent variables:	age sex S/A W/S	
Dependent variable:	total leucocyte count	
No variables entered		
Dependent variable:	total lymphocyte count	
Variables entered:		
	r^2	*P*
Z S/A	0.08	<.10
Age	0.11 (negative)	<.05
Taller children have higher lymphocyte count		
Dependent variable:	neutrophil count	
Variables entered:		
	r^2	*P*
Z W/S	0.08	<.10
As nutritional status improves, neutrophil count goes up		
Dependent variable:	monocytes, eosinophils, and basophils combined	
Variables entered:		
	r^2	*P*
Age	0.13 (negative)	<.05

older children of lower stature having lower counts. Neutrophil count was significantly associated with Z W/S, children with greater Z W/S having higher counts. Combined monocyte, eosinophil, and basophil count was negatively associated with age only.

DISCUSSION

In this population, there is poor growth performance and nutritional stunting and wasting, but no reduction in leucocyte count, as might be predicted from accounts of the immunosuppressive effects of undernutrition (e.g., Chandra and Scrimshaw, 1980; Gibson, 1990). However, within the sample, poorer growth (Z S/A) is associated with lower total lymphocyte count against a background of elevated levels relative to western reference values among the older children, whereas poorer current nutritional status (Z W/S) is associated with lower neutrophil count, against a background of normal neutrophil levels across all age groups. Total lymphocyte count and combined monocyte, eosinophil, and basophil counts show positive and independent associations with age.

Although children with clinical signs of infection were excluded from the sample, it is possible that the general lack of immunosuppression is due to the high infectious loads that Anga children habitually experience. Pneumonia, malaria, and intestinal infections are the three leading causes of morbidity in children under 9 years of age in Papua New Guinea (Policy Planning and Evaluation Division, Papua New Guinea Ministry of Health, 1990). Pneumonia is a common disease of childhood in less-developed countries, and malaria has become so among highland fringe populations such as the Anga. Malarial transmission has increased in highland and highland fringe areas of the country as road and air communications have improved (Radford et al., 1976). Hookworm is widespread throughout PNG and is common in the Anga population (Barnish and Ashford, 1989). The prevalence of hookworm rises with age from approximately 1 year of age, until a plateau of about 70–80% prevalence is reached between the ages of 8 and 10 years (Barnish and Ashford, 1989). *Ascaris* is also present in the Anga population, whereas *Trichuris* is not (Barnish and Ashford, 1990). Although worm loads were not measured in this study, they are likely to have been high, and it is likely that the Anga experience of chronic parasitic infections would involve persistent antigenic stimulation. The splenomegaly and hepatomegaly characteristic of malaria is associated with increased numbers and activity of macrophages and lymphocytes in the liver and spleen; the higher-than-expected lymphocyte count in the 2–7 years age group may be a function of this, and differentially poor growth within the sample is also associated with lower lymphocyte count relative to members of the group who are taller for age. The highly elevated number of monocytes, eosinophils, and basophils may also reflect

the physiological and immunological changes associated with adaptation to malaria infection, if the count reflects an increase in monocyte number with age. In a study of PNG highlanders, Witt and Alpers (1991a) showed 30% elevation in total lymphocyte numbers relative to reference values in the age group 0–5 months, but with a value slightly lower than the reference figure in the age group 6–14 months. These authors do not report values for children in the next age group, but children aged 10–15 years have total lymphocyte values which are about 50% above the reference figure, most of this elevation being in the CD8 cell count. The authors relate this to experience of pneumonia (Witt and Alpers, 1991b), although exposure to other infectious agents was not controlled for.

Eosinophils are major effector cells against helminths, and the T-cell-dependent increase in these cells may be associated with chronic ascariasis and hookworm infection. In the present sample, the sum of monocytes, eosinophils, and basophils more than doubles the reference value in the younger age group and nearly trebles the reference value in the older age group. Furthermore, this count is associated with age, but neither nutritional status nor relative stature. If these values represent elevated eosinophil numbers, it might suggest immunological response to chronic helminthic infection, perhaps increasing with age as prevalence of hookworm and ascariasis increase with age (Barnish and Ashford, 1989; Bundy and Medley, 1992), but independently of nutritional status or growth faltering. This remains to be tested, as the present study did not measure worm burden.

Relative to western reference values, growth faltering and age-related immunological elevation are norms in the present study, although relative immunosuppression of two immune system components is present among the most stunted and wasted of the sample. The small group of children with very high leucocyte counts (>15,000) have significantly lower Z S/A ($P < .001$) and Z W/S ($P < .02$) than children with leucocyte counts below 15,000. This seemingly paradoxical effect might reflect associations between immunological variables and anthropometric nutritional status that could not be teased out with the small sample size of the present study. The high leucocyte count group is slightly older and has a slightly lower count of lymphocytes, and of monocytes, eosinophils, and basophils combined, and a higher neutrophil count than the low leucocyte count group. This follows the more general age trend in leucocyte subsets reported in Table 2 and may reflect survivorship within the young child population rather than indicate direct association between undernutrition and elevated immune status.

The pattern of weight and stature growth seen in the Anga may reflect extended nutritional deficits which result in stunting of a degree to which the most growth-compromised children die, leaving those above a threshold associated with high mortality alive (Ulijaszek, 1996). Certainly, child deaths among the Anga people of Gulf, Morobe, and Eastern Highlands Provinces are reported at 327/1,000 live births (Leonard et al., 1988) whereas for the Bundi it was 177/1,000 (Malcolm, 1970). Comparisons of height, length, and weight by age of Anga (Ulijaszek, 1981) and Bundi (Malcolm, 1970) children below the age of 3 years shows the Anga children to become marginally shorter than the Bundi after the age of 12 months, and lighter across the entire age range. Various studies of prospective mortality have been carried out in relation to anthropometric status, and most have shown greater risk of death among children who were either light for age or stature or short for age (Pelletier, 1991). In PNG, Heywood (1982) reported clear and significantly higher 2-year mortality in children with low weight for age, weight for height, and height for age among a group of 1,232 children aged 6–30 months at the start of the study, and followed prospectively. Similar results have been reported for Bangladesh (Chen et al., 1980; Coghill, 1982; Alam et al., 1989). The comparison of younger and older Anga children in the present study may reflect population differences, inasmuch as the children aged 2–7 years are survivors of nutritional and infectious disease stresses. Thus, the anthropometric and immunological characteristics of the older age group may reflect

the biology of survivorship under severe ecological conditions, where poor linear growth and elevated leucocyte status are characteristics of survivorship.

LITERATURE CITED

Alam N, Rahaman MM, and Wojtyniak B (1989) Anthropometric indicators and risk of death. Am. J. Clin. Nutr. *49:*884–888.

Ashford RW, Hall AJ, and Babona D (1981) Distribution and abundance of intestinal helminths in man in western Papua New Guinea with special reference to *Strongyloides.* Ann. Trop. Med. Parasitol. *75:*269–279.

Barnish G and Ashford RW (1989) *Strongyloides cf. fuelleborni* and hookworm in Papua New Guinea: patterns of infection within the community. Trans. R. Soc. Med. Hyg. *83:*684–688.

Barnish G and Ashford RW (1990) *Strongyloides cf. fuelleborni* and other intestinal helminths in Papua New Guinea: distribution according to environmental factors. Parasitologia *32:*245–263.

Bundy DAP and Medley GF (1992) Immuno-epidemiology of human geohelminthiasis: ecological and immunological determinants of worm burden. Parasitology *104:*S105–S119.

Cattani J (1992) The epidemiology of malaria in Papua New Guinea. In RD Attenborough and MP Alpers (eds.): Human Biology in Papua New Guinea. Oxford: Oxford University Press, pp. 302–312.

Chandra RK and Scrimshaw NS (1980) Immunocompetence in nutritional assessment. Am. J. Clin. Nutr. *33:*2694–2697.

Chen LC, Alauddin Chowdhury AKM, and Huffman SL (1980) Anthropometric assessment of energy-protein malnutrition and subsequent risk of mortality among preschool aged children. Am. J. Clin. Nutr. *33:*1836–1845.

Coghill B (1982) Ranking anthropometric indicators using mortality in rural Bangladeshi children. Cornell University: PhD thesis.

Gibson RS (1990) Principles of Nutritional Assessment. Oxford: Oxford University Press.

Heywood PF (1982) The functional significance of malnutrition: growth and prospective risk of death in the Highlands of Papua New Guinea. J. Food Nutr. *39:* 13–19.

Heywood PF (1985) 1983 National Nutrition Survey—Preliminary District Level Analysis of Length and Weight Data. (Goroka: Papua New Guinea Institute of Medical Research Report).

Lentner C (1984) Geigy Scientific Tables, Vol. 3. Physical Chemistry, Composition of Blood, Hematology, Somatometric Data. Basel: Ciba-Geigy.

Leonard D, Manning LA, and Dockery GD (1988) Mortality experienced by children of the Anga region of Papua New Guinea. PNG Med. J. *31:*39–44.

Malcolm LA (1970) Growth and Development in New Guinea—A Study of the Bundi People of the Madang District. Madang: Institute of Human Biology.

National Centre for Health Statistics (1977) NCHS Growth Curves for Children. Publication No. (PHS) 78-1650. Hyattsville, MD: United States Department of Health, Education and Welfare.

Pelletier DL (1991) Relationships Between Child Anthropometry and Mortality in Developing Countries: Implications for Policy, Programs, and Future Research. Ithaca, NY: Cornell Food and Nutrition Policy Program Monograph No. 12.

Policy Planning and Evaluation Division (1990) Handbook of Health Statistics, Papua New Guinea, 1990. Port Moresby: Papua New Guinea Ministry of Health.

Radford AJ, van Leeuwen H, and Christian SH (1976) Social aspects in the changing epidemiology of malaria in the highlands of New Guinea. Ann Trop. Med. Parasitol. *70:*11–23.

Riley ID, Lehmann D, and Alpers MP (1992). Acute respiratory infections. In RD Attenborough and MP Alpers (eds): Human Biology in Papua New Guinea. Oxford: Oxford University Press, pp. 281–288.

Saweri W (1995) Report of Kaintiba Nutrition and Health Survey, 1992–1993. Port Moresby: Smallholders Market and Food Supply Project.

Ulijaszek SJ (1981) Weights and Heights of the Kapau Anga Population of Gulf Province, Papua New Guinea. Port Moresby: Department of Public Health Report.

Ulijaszek SJ (1996) Age of eruption of deciduous dentition of Anga children, Papua New Guinea. Ann. Hum. Biol. *23:*495–499.

Weiner JS and Lourie JA (1981) Practical Human Biology. London: Academic Press.

Witt CS and Alpers MP (1991a) Lymphocyte subsets in Eastern Highlanders of Papua New Guinea. PNG Med. J. *34:*98–103.

Witt CS and Alpers MP (1991b) Impaired cell-mediated immunity in Papua New Guinean infants. PNG Med. J. *34:*90–97.